REMARKS

Claims 10–26 and 29 are currently pending in this application. In response to the Final Action, Applicant respectfully requests entry of the claim amendments presented herein and further consideration of the present application in view of these amendments and the remarks provided below.

Support for Claim Amendments

The amendments presented herein have been made to recite particular aspects of the invention so as to expedite the prosecution of the present application to allowance in accordance with the USPTO Patent Business Goals (65 Fed. Reg. 54603, September 8, 2000). These amendments do not represent an acquiescence or agreement with any of the outstanding rejections.

Claim 10 is amended herein, incorporating all the recitations of claim 17. In view of this amendment, claims 19–23 are amended herein to change claim dependency and claims 17, 18 and 24–26 are canceled herein without prejudice. Lastly, claim 29 is amended herein to correct a typographical error. Support for these claim amendments can be found in the application and claims as originally filed. The points raised by the Examiner are addressed hereinbelow.

Claim Rejections, 35 U.S.C. § 103(a)

Claims 10–26 and 29 stand rejected unde 35 U.S.C. § 103(a) as being unpatentable over U.S. Application Publication No. 2001/0034340 ("Pickar") in view of U.S. Patent No. 5,798,347 ("Labrie"), U.S. Patent No. 4,381,298 ("Coulson"), Prestwood et al. (2000) *J. Clin. Endocrinol. Metab.* 85:4462–4469 ("Prestwood et al."), and Utian et al. (1999) *A. J Obstet. Gynecol.* 181:71–79 ("Utian et al.").

It is the assertion of the Examiner that it would have been obvious to the skilled artisan at the time the invention was made to treat vasomotor symptoms by a method comprising a first dose of a therapeutic amount of an estrogenic compound to a subject; and administering a second dose of a therapeutic amount of an estrogenic compound at a later time period to the subject, said second dose comprising a lower dosage of said therpapeutic amount of an estrogenic compound

than said first dose to produce the required effect, i.e., to treat vasomotor symptoms in view of the teachings of Prestwood et al. and Utian et al. Applicant respectfully traverses this rejection.

Applicant respectfully points out that, as stated in the recently published Examination Guidelines for Determining Obviousness, "the Supreme Court reaffirmed the familiar framework for determining obviousness as set forth in *Graham v. John Deere Co....*" (Examination Guidelines for Determining Obviousness Under 35 U.S.C § 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register Vol. 72, No. 195, 57526-57535, 57526). Hence, and as long established under that framework, to establish a *prima facie* case of obviousness, three requirements must be satisfied (M.P.E.P. § 2143). First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. *In re Oetiker,* 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Second, the proposed modification or combination of the prior art must have a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Third, the prior art reference or combination of references must teach or suggest all of the limitations of the claims. *See In re Wilson* 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (CCPA 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art").

Furthermore, the Court of Appeals for the Federal Circuit has also stated that, to support combining or modifying references, there must be particular evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Furthermore, as affirmed by the Court of Appeals for the Federal Circuit in *In re Sang-su Lee*, a factual question of motivation is material to patentability, and cannot be resolved on subjective belief and unknown authority. *See In re Sang-su Lee*, 277 F.3d 1338 (Fed. Cir. 2002).

The claims as amended herein are directed toward a method of treating vasomotor symptoms comprising the administering of a first high dose of a therapeutic amount of an

estrogenic compound, followed by the administering of a second, lower dose of a therapeutic amount of an estrogenic compound and administering a therapeutic amount of a progestational agent. The disclosures of Utian et al. suggest that based on their studies, "[a] logical approach is to initiate treatment with a low dose of estradiol, which is more likely to provide an acceptable level of relief from vasomotor symptoms while minimizing the signs of hyperestrogenism." (p. 78 col. 2 lines 17–20). In contrast, the disclosures of Prestwood et al. point out that, "[i]n younger postmenopausal women, the use of lower doses of estrogen may not be as effective in preventing bone loss." (p. 4467 col. 1 lines 8–10). As such, the disclosures of Utian et al. appear to teach away from starting estrogen replacement therapy (ERT) treatments with high doses of estrogenic compounds, whereas the disclosures of Prestwood et al. appear to indicate that ERT treatments with low doses of estrogenic compounds may not be effective in younger postmenopausal women.

Although the disclosures of Pickar may disclose that the dosage may need to be adjusted up or down during the treatment period, the disclosures of Pickar fail to explicitly teach a method of treating vasomotor symptoms comprising administering a high first dose of an estrogenic compound and a second dose of an estrogenic compound, wherein the second dose of an estrogenic compound is lower than the first dose. Furthermore, in view of the remarks above regarding the disclosures of Utian et al. and Prestwood et al., Applicant presents that disclosures of Utian et al. and Prestwood et al. do not suggest that it would have been obvious to one of ordinary skill in the art to administer a high first dose of an estrogenic compound followed by a lower second dose of an estrogenic compound. The disclosures of Labrie and Coulson, relied on solely to show that medroxyprogesterone acetate is a progestin and an androgen respectively, do not cure the deficiencies in the teachings of Pickar, Utian et al. and Prestwood et al. in regard to rendering the claimed invention obvious over the cited references.

In view of the foregoing, Applicant presents that the instant claims are not obvious over the prior art, to which Applicant respectfully requests that the instant rejection be withdrawn.

Double Patenting

Claims 10–18, 24 and 25 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1–7 of co-pending U.S. Application Serial No. 10/678,828 ("the '828 Application"), and claim 10 is also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 6 of co-pending U.S. Application Serial No. 10/356,242 ("the '242 Application"). Applicants will timely file a terminal disclaimer should either the '828 Application or the '242 Application issue prior to the present application and once the instant claims have been allowed.

CONCLUSION

Applicant believes that the points and concerns raised by the Examiner in the Action have been addressed in full, it is respectfully submitted that this application is in condition for allowance. Should the Examiner have any remaining concerns, it is respectfully requested that the Examiner contact the undersigned Attorney at (919) 854-1400 to expedite the prosecution of this application to allowance.

A Petition for Extension of Time is included with this response for a one-month extension of time. Applicant authorizes the Commissioner to charge Deposit Account No. 50-0220 in the amount of $120 as fee for this extension. Applicant believes this amount to be correct; however, the Commissioner is hereby authorized to charge any deficiency or credit any refund to Deposit Account No. 50-0220.

Respectfully submitted,

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CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on August 29, 2008.

Tracy Wallace